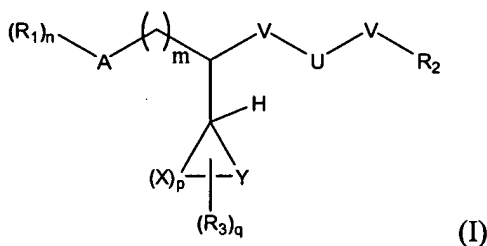


We claim:

1. A method for enhancing memory in an animal, comprising administering to the animal a formulation of one or more methylphenidate compounds, or pharmaceutically acceptable derivative, salt, solvate, pro-drug or metabolic derivative thereof, in an amount sufficient to enhance long-term memory in the animal, wherein the formulation includes at least 60 mol percent of a eutomer(s) relative to the distomer(s) of the methylphenidate compound(s).

2. The method of claim 1, wherein the formulation includes at least 60 percent (w/w) of a eutomer(s) of methylphenidate compound(s) represented by the general formula:



wherein

A represents a carbocyclic, heterocyclic, aryl, or heteroaryl ring;

U is absent or represents -C(=O)-, -C(=S)-, -P(=O)(OR₈)-, -S(O₂)-, or -S(O)-;

V, independently for each occurrence, is absent or represents NR, O, or S;

Y represents NR₄, O, or S;

each occurrence of X, independently, is an atom selected from C, N, S, Se, and O;

R, independently for each occurrence, represents H, lower alkyl, lower alkenyl, aryl, heteroaryl, aralkyl, or heteroaralkyl;

each occurrence of R₁ represents, independently, aryl, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 acyloxy, hydroxyl, C1-C6 alkanoyl, halogen, cyano,

carboxyl, amido, amino, C1-C6 acylamino, C1-C6 alkylamino, nitro, sulfonic acid, or sulfhydryl;

R₂ is selected from H, C1-C6 alkyl, and C1-C6 alkanoyl;

5 R₃ represents, independently for each occurrence, hydrogen, C1-C6 alkyl, C1-C6 alkoxy, hydroxyl, C1-C6 alkanoyl, halogen, carboxyl, C2-C6 alkanoxy, nitro, or sulfhydryl, or two of R₃, taken together, represent an oxo group or a double bond between two adjacent X atoms;

R₄ represents hydrogen, lower alkyl, acyl, aryl, aralkyl, heteroaryl, or heteroaralkyl, preferably hydrogen or lower alkyl;

10 R₈ represents hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

m is an integer selected from 0 and 1;

n is an integer from 0 to 7;

p is an integer selected from 3, 4, 5, and 6; and

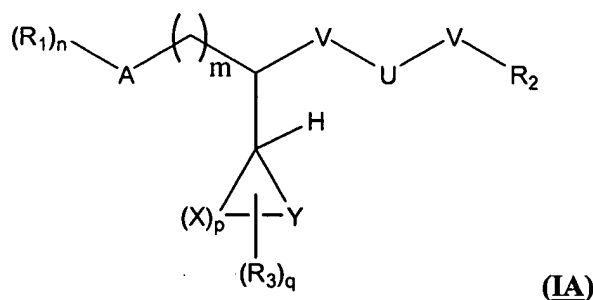
15 q is an integer from 0 to 16; or

a pharmaceutically acceptable derivative, salt, solvate, pro-drug or metabolic derivative thereof.

3. A method for enhancing memory in an animal, comprising administering to the animal a formulation of a methylphenidate compound, or pharmaceutically acceptable derivative, salt, solvate, pro-drug or metabolic derivative thereof, in an amount sufficient to enhance long-term memory in the animal, wherein the formulation includes at least 60 percent (w/w) of the eutomer(s) relative to the distomer(s) of the methylphenidate compound(s).

20

25 4. The method of claim 3, wherein the eutomer of the methylphenidate compound is a compound represented in the general formula (IA), or pharmaceutically acceptable salt, pro-drug or metabolic derivative thereof:



wherein

A represents a carbocyclic, heterocyclic, aryl, or heteroaryl ring;

U is absent or represents -C(=O)-, -C(=S)-, -P(=O)(OR₈)-, -S(O₂)-, or -S(O)-;

V, independently for each occurrence, is absent or represents NR, O, or S;

Y represents NR₄, O, or S;

each occurrence of X, independently, is an atom selected from C, N, S, Se, and O;

R, independently for each occurrence, represents H, lower alkyl, lower alkenyl, aryl, heteroaryl, aralkyl, or heteroaralkyl;

each occurrence of R₁ represents, independently, aryl, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 acyloxy, hydroxyl, C1-C6 alkanoyl, halogen, cyano, carboxyl, amido, amino, C1-C6 acylamino, C1-C6 alkylamino, nitro, sulfonic acid, or sulfhydryl;

R₂ is selected from H, C1-C6 alkyl, and C1-C6 alkanoyl;

R₃ represents, independently for each occurrence, hydrogen, C1-C6 alkyl, C1-C6 alkoxy, hydroxyl, C1-C6 alkanoyl, halogen, carboxyl, C2-C6 alkanoxy, nitro, or sulfhydryl, or two of R₃, taken together, represent an oxo group or a double bond between two adjacent X atoms;

R₄ represents hydrogen, lower alkyl, acyl, aryl, aralkyl, heteroaryl, or heteroaralkyl, preferably hydrogen or lower alkyl;

m is an integer selected from 0 and 1;

n is an integer from 0 to 7;

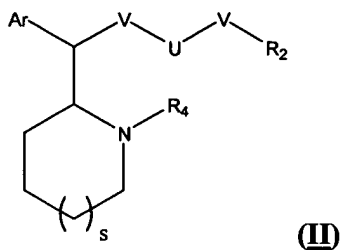
p is an integer selected from 3, 4, 5, and 6; and

q is an integer from 0 to 16, or

a pharmaceutically acceptable derivative, salt, solvate, pro-drug or metabolic derivative thereof.

5

5. The method of claim 3, wherein the eutomer of the methylphenidate compound is represented in the general formula (II), or pharmaceutically acceptable salt, pro-drug or metabolic derivative thereof:



10

wherein

U is absent or represents -C(=O)-, -C(=S)-, -P(=O)(OR₈)-, -S(O₂)-, or -S(O)-;

15

V, independently for each occurrence, is absent or represents NR, O, or S;

R, independently for each occurrence, represents H, lower alkyl, lower alkenyl, aryl, heteroaryl, aralkyl, or heteroaralkyl;

R₂ is selected from H, C1-C6 alkyl, and C1-C6 alkanoyl;

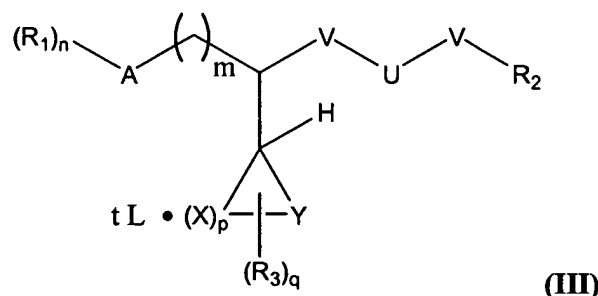
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R₄ represents hydrogen, lower alkyl, acyl, aryl, aralkyl, heteroaryl, or heteroaralkyl, preferably hydrogen or lower alkyl;

s represents an integer from 0 to 2; and

Ar represents a substituted or unsubstituted aryl or heteroaryl group.

6. The method of claim 3, wherein the pharmaceutically acceptable salt of the enantiomer of the methylphenidate compound has a structure represented in the general formula (III):



wherein

A represents a carbocyclic, heterocyclic, aryl, or heteroaryl ring;

U is absent or represents $-\text{C}(=\text{O})-$, $-\text{C}(=\text{S})-$, $-\text{P}(=\text{O})(\text{OR}_8)-$, $-\text{S}(\text{O}_2)-$, or $-\text{S}(\text{O})-$;

V, independently for each occurrence, is absent or represents NR , O, or S;

Y represents NR_4 , O, or S;

each occurrence of X, independently, is an atom selected from C, N, S, Se, and O;

R, independently for each occurrence, represents H, lower alkyl, lower alkenyl, aryl, heteroaryl, aralkyl, or heteroaralkyl;

each occurrence of R_1 represents, independently, aryl, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 acyloxy, hydroxyl, C1-C6 alkanoyl, halogen, cyano, carboxyl, amido, amino, C1-C6 acylamino, C1-C6 alkylamino, nitro, sulfonic acid, or sulfhydryl;

R_2 is selected from H, C1-C6 alkyl, and C1-C6 alkanoyl;

R_3 represents, independently for each occurrence, hydrogen, C1-C6 alkyl, C1-C6 alkoxy, hydroxyl, C1-C6 alkanoyl, halogen, carboxyl, C2-C6

alkanoxy, nitro, or sulfhydryl, or two of R₃, taken together, represent an oxo group or a double bond between two adjacent X atoms;

R₄ represents hydrogen, lower alkyl, acyl, amido, ester, aryl, aralkyl, heteroaryl, or heteroaralkyl, preferably hydrogen or lower alkyl;

5 m is an integer selected from 0 and 1;

n is an integer from 0 to 7;

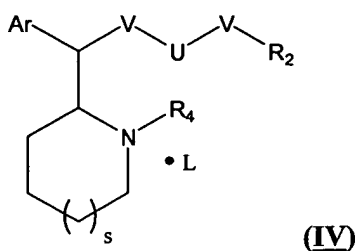
p is an integer selected from 3, 4, 5, and 6; and

q is an integer from 0 to 16;

10 L is a non-toxic organic or inorganic acid, or a quaternizing agent, or any combination thereof; and

t is an integer from 1 to 6.

- 15 7. The method of claim 3, wherein the pharmaceutically acceptable salt of the enantiomer of the methylphenidate compound has a structure represented in the general formula (IV), or a pharmaceutically acceptable salt, solvate or pro-drug thereof:



wherein

20 U is absent or represents -C(=O)-, -C(=S)-, -P(=O)(OR₈)-, -S(O₂)-, or -S(O)-;

V, independently for each occurrence, is absent or represents NR, O, or S;

25 R, independently for each occurrence, represents H, lower alkyl, lower alkenyl, aryl, heteroaryl, aralkyl, or heteroaralkyl;

R₂ is selected from H, C1-C6 alkyl, and C1-C6 alkanoyl;

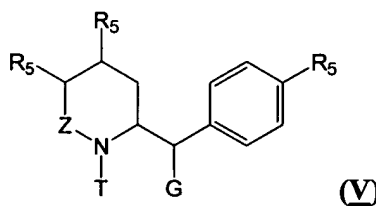
R₄ represents hydrogen, lower alkyl, acyl, aryl, aralkyl, heteroaryl, or heteroaralkyl, preferably hydrogen or lower alkyl;

s represents an integer from 0 to 2;

5 Ar represents a substituted or unsubstituted aryl or heteroaryl group;
and

L is a non-toxic organic or inorganic acid, or a quaternizing agent, or any combination thereof.

- 10 8. The method of claim 3, wherein the metabolite of the eutomer of the methylphenidate compound has a structure represented in the general formula (V), or a pharmaceutically acceptable salt, solvate or pro-drug thereof:



15 wherein

R₅, independently for each occurrence, is absent or represents hydroxyl;

Z represents -CH₂- or -C(=O)-;

T represents hydrogen or -C(=O)-NH₂;

20 G represents carboxylic acid, or a pharmaceutically acceptable salt thereof, carboxylic acid methyl ester, carboxylic acid ethyl ester, or acetylamino ethane sulfonic acid.

- 25 9. The method of any of claims 4, 5, 6, 7 or 8, wherein R₂ represents H or C1-C6 alkyl.

10. The method of any of claims 4, 5, 6, 7 or 8, wherein U represents $-C(=O)-$ or $-C(=S)-$.

5 11. The method of any of claims 4, 5, 6, 7 or 8, wherein at least one occurrence of V is present.

12. The method of claim 11, wherein V is absent for one occurrence, and in the other V represents NH, S, or O.

10 13. The method of claim 4 or 6, wherein A represents an aryl or heteroaryl group.

15 14. A pharmaceutical preparation comprising a methylphenidate compound in an amount sufficient to enhance long-term memory in the animal, wherein the preparation includes at least 60 percent (w/w) of the eutomer(s) relative to the distomer(s) of the methylphenidate compound(s).

20 15. A single dosage pharmaceutical preparation for oral administration to a human patient, comprising one or more methylphenidate compounds in an amount sufficient to enhance long-term memory in the animal, wherein the preparation includes at least 60 percent (w/w) of the eutomer(s) relative to the distomer(s) of the methylphenidate compound(s), and is formulated for delivering a sustained and increasing dose over at least 4 hours to lessen the incidence of tolerance in the patient.

25 16. The preparation of claim 15, for delivering a sustained and increasing dose over at least 8 hours.

17. The preparation of claim 15, comprising a multiplicity of layers each including the same or different polymers, a dose of the methylphenidate compound(s) in

an increasing dose in the multiplicity of layers, wherein in operation the preparation delivers an increasing dose of the methylphenidate compound(s) over time.

5 18. The preparation of claim 15, comprising a bioerodible polymer, a dose of the methylphenidate compound(s) present in an initial dose and a final dose, whereby the preparation delivers an initial dose then a final dose over time.

10 19. The preparation of claim 15, comprising a plurality of beads, each bead including a methylphenidate compound and having a dissolution profile, which plurality of beads is a variegated population with respect to dose and/or dissolution profile so as deliver, upon administration, said sustained and increasing dose over at least 4 hours

15 20. The preparation of claim 15, wherein the methylphenidate compound is (i) contained within a nonabsorbable shell that releases the drug at a controlled rate, and (i) formulated in at least two different dissolution profiles.

20 21. A kit comprising:
a. a pharmaceutical preparation comprising a methylphenidate compound in an amount sufficient to enhance long-term memory in the animal, wherein the preparation includes at least 60 percent (w/w) of a eutomer(s) relative to a distomer(s) of the methylphenidate compound(s); and
25 b. instructions, written and/or pictorial, describing the use of the preparation for enhancing memory in a patient.

22. The kit of claim 21, wherein the methylphenidate compound is provided in single dosage form.

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23. The kit of claim 22, wherein the methylphenidate compound is formulated for delivering a sustained and increasing dose over at least 4 hours to lessen the incidence of tolerance in the patient.

5 24. The kit of claim 21, wherein the methylphenidate compound is provided in the form of a transdermal patch.

25. The method of claim 1 or 3, the preparation of claim 14 or 15 or the kit of claim 21, wherein said methylphenidate compound(s) is provided in an amount sufficient to enhance long-term memory in a patient by a statistically significant amount when assessed by a standardized performance test.

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26. The method, preparation or kit of claim 25, wherein said standardized test is selected from the group consisting of: Cambridge Neuropsychological Test Automated Battery (CANTAB); a Children's Memory Scale (CMS); a Contextual Memory Test; a Continuous Recognition Memory Test (CMRT); a Denman Neuropsychology Memory Scale; a Fuld Object Memory Evaluation (FOME); a Graham-Kendall Memory for Designs Test; a Guild Memory Test; a Learning and Memory Battery (LAMB); Rey Auditory and Verbal learning Test (RAVLT); Brief Visuospatial Memory Test (BVRT); Providence Recognition Memory Test (PRMT), a Memory Assessment Clinic Self-Rating Scale (MAC-S); a Memory Assessment Scales (MAS); a Randt Memory Test; a Recognition Memory Test (RMT); a Rivermead Behavioral Memory Test; a Russell's Version of the Wechsler Memory Scale (RWMS); a Test of Memory and Learning (TOMAL); a Vermont Memory Scale (VMS); a Wechsler Memory Scale; and a Wide Range Assessment of Memory and Learning (WRAML).

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27. The method, preparation or kit of claim 25, wherein said standardized test is a Providence Recognition Memory Test.

28. The method of claim 1 or 3, further comprising administering one or more of a neuronal growth factor, a neuronal survival factor, a neuronal trophic factor, a

cholinergic modulator, an adrenergic modulator, a nonadrenergic modulator, a dopaminergic modulator, a glutaminergic modulator or an agent that stimulates the PKC, PKA, GABA, NMDA, cannabinoid, AMPA, kainate, phosphodiesterase (PDE), CREB or nootropic pathways.

- 5 29. The method of claim 1 or 3, the preparation of claim 14 or 15 or the kit of claim 21, for use in the prophylaxis or treatment of a patient susceptible to or suffering from memory impairment.
- 10 30. The method, preparation or kit of claim 29, for use in the prophylaxis or treatment of a patient susceptible to or suffering from impaired memory due to anxiety, depression, age-associated memory impairment, minimal cognitive impairment, amnesia, dementia, learning disabilities, memory impairment associated with toxicant exposure, brain injury, brain aneurysm, Parkinson's disease, head trauma, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, stroke, schizophrenia, epilepsy, mental retardation, Alzheimer's disease, age, attention deficit disorder, attention deficit hyperactivity disorder, AIDS-related dementia, sleep deprivation, a sleep disorder.
- 15 31. The method of claim 1 or 3, the preparation of claim 14 or 15 or the kit of claim 21, for enhancing memory in normal individuals.
- 20 32. A method for conducting a pharmaceutical business, comprising:
a. manufacturing a preparation of claims 14 or 15; and
b. marketing to healthcare providers the benefits of using the preparation to increase memory function.
- 25 33. A method for conducting a pharmaceutical business, comprising:
a. providing a distribution network for selling the preparation of claims 14 or 15; and
b. providing instruction material to patients or physicians for using the preparation to increase memory function.

34. A method for conducting a pharmaceutical business, comprising:
- a. determining an appropriate preparation and dosage of a methylphenidate compound to increase memory function;
 - 5 b. conducting therapeutic profiling of preparations identified in step (a), for efficacy and toxicity in animals; and
 - c. providing a distribution network for selling a preparation identified in step (b) as having an acceptable therapeutic profile.

- 10 35. The method of claim 34, including an additional step of providing a sales group for marketing the preparation to healthcare providers.

36. A method for conducting a pharmaceutical business, comprising:
- a. determining an appropriate preparation and dosage of methylphenidate to be administered to increase memory function; and
 - 15 b. licensing, to a third party, the rights for further development and sale of the preparation.
37. Specific treatment for ADD.

- 20 37. A method for enhancing attention span in an animal, comprising administering to the animal a formulation of one or more methylphenidate compounds, or pharmaceutically acceptable derivative, salt, solvate, pro-drug or metabolic derivative thereof, in an amount sufficient to enhance attention span in the animal, wherein the formulation includes at least 60 percent (w/w) of a L-threo (2S:2'S) stereoisomer, a D-threo (2R:2'R) stereoisomer, or a
- 25 combination thereof of the methylphenidate compound relative to erythroisomers of the methylphenidate compound.

38. The method of claim 37, wherein the animal has a condition characterized by a deficit in attention span.

39. The method of claim 38, wherein the condition is selected from the group consisting of Attention Deficit Disorder, Attention Deficit Disorder with Hyperactivity, Tourette's Syndrome, autism, depression, and bi-polar disorder.

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40. The method of claim 38, wherein the condition is selected is selected from the group consisting of Attention Deficit Disorder and Attention Deficit Disorder.

41. A method for ^(treating) Attention Deficit Disorder (ADD) or Attention Deficit Disorder with Hyperactivity (ADHD) in an animal, comprising administering to the animal a formulation of one or more methylphenidate compounds, or pharmaceutically acceptable derivative, salt, solvate, pro-drug or metabolic derivative thereof, wherein the formulation includes at least 60 percent (w/w) of a L-threo (2S:2'S) stereoisomer, a D-threo (2R:2'R) stereoisomer, or a combination thereof of the methylphenidate compound relative to erythro-isomers of the methylphenidate compound.

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42. A method of enhancing attention span in a patient, comprising administering the pharmaceutical preparation of claim 14 or 15.

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43. A method for treating a condition characterized by a deficit in attention span, comprising administering the pharmaceutical preparation of claim 14 or 15.

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44. A single dose formulation of one or more methylphenidate compounds, wherein the single dose is greater than 60 mg.

44. The formulation of claim 43, wherein the single dose is greater than 100 mg.

45. The formulation of claim 44, wherein the single dose is greater than 250 mg.

46. The formulation of claim 45, wherein the single dose is greater than 500 mg.

5 47. The method of claim 3, wherein the formulation includes at least at least 60 percent (w/w) of a L-threo (2S:2'S) stereoisomer of methylphenidate relative to D-threo (2R:2'R), D-erythro (2R:2'S) and L-erythro (2S:2'R) isomers of methylphenidate.

10 48. The pharmaceutical preparation of claim 14, wherein the preparation includes at least 60 percent (w/w) of a L-threo (2S:2'S) stereoisomer, a D-threo (2R:2'R) stereoisomer, or a combination thereof of methylphenidate relative to erythro-isomers of methylphenidate.

15 49. The single dosage pharmaceutical preparation of claim 15, wherein the preparation includes at least 60 percent (w/w) of a L-threo (2S:2'S) stereoisomer, a D-threo (2R:2'R) stereoisomer, or a combination thereof of methylphenidate relative to erythro-isomers of methylphenidate.

20 50. The kit of claim 21, wherein the preparation includes at least 60 percent (w/w) of a L-threo (2S:2'S) stereoisomer, a D-threo (2R:2'R) stereoisomer, or a combination thereof of methylphenidate relative to erythro-isomers of methylphenidate.

25